

SEQUENCE LISTING

<110> POLONSKY, KENNETH S.
 HORIKAWA, YUKIO
 ODA, NAOHISA
 COX, NANCY J.
 SREENAN, SEAMUS
 ZHOU, YUN-PING
 OTANI, KENICHI
 HANIS, CRAIG L.
 BELL, GRAEME I.

<120> METHODS OF TREATMENT OF TYPE 2 DIABETES

<130> ARCD:307

<140> UNKNOWN

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<150> 60/134,175

<151> 1999-05-13

60/105,052

1998-10-21

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<170> PatentIn Ver. 2.0

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Pro	Leu	Ala	Gln	Phe	Arg	Glu	Asp	Ile	Thr	Trp	Arg	Arg	Pro	Gln	Glu	35	40	45	
Ile	Cys	Ala	Thr	Pro	Arg	Leu	Phe	Pro	Asp	Asp	Pro	Arg	Glu	Gly	Gln	50	55	60	
Val	Lys	Gln	Gly	Leu	Leu	Gly	Asp	Cys	Trp	Phe	Leu	Cys	Ala	Cys	Ala	65	70	75	80
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Gln	Pro	Ser	Trp	Ala	Asp	Gln	Glu	Tyr	Arg	Gly	Ser	Phe	Thr	Cys	Arg	100	105	110	
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Pro	Cys	Leu	Ala	Gly	Arg	Leu	Cys	Phe	Ser	Arg	Cys	Gln	Arg	Glu	Asp	130	135	140	
Val	Phe	Trp	Leu	Pro	Leu	Leu	Glu	Lys	Val	Tyr	Ala	Lys	Val	His	Gly	145	150	155	160
Ser	Tyr	Glu	His	Leu	Trp	Ala	Gly	Gln	Val	Ala	Asp	Ala	Leu	Val	Asp	165	170	175	
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Ile	Val	Ser	Asp	Leu	Arg	Glu	Leu	Gln	Gly	Gln	Ala	Gly	Gln	Cys	Ile	245	250	255	
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 Tyr Gln Ala Val Gly Leu His Leu Trp Lys Val Glu Lys Arg Arg Val
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 Ala Gln Glu Val Ser Arg Leu Cys Leu Leu Pro Ala Gly Thr Tyr Lys
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 Val Val Pro Ser Thr Tyr Leu Pro Asp Thr Glu Gly Ala Phe Thr Val
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Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
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Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
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Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
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Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
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Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp
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Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
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Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
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Leu Thr Gly Gly Leu Ala Glu Arg Trp Asn Leu Lys Gly Val Ala Gly
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Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
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Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
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Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
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Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
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Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
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Ser Gly Gly Gln Gln Asp Arg Pro Gly Arg Trp Glu His Arg Thr Cys
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225 230 235 240
Ile Val Ser Asp Leu Arg Glu Leu Gln Gly Gln Ala Gly Gln Cys Ile
245 250 255

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 Gly Ala Phe Thr Val Thr Ile Ala Thr Arg Ile Asp Arg Pro Ser Ile
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 <213> Human

<400> 7

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<210> 8

<211> 513

<212> PRT

<213> Human

<400> 8

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Ala Ala Phe Pro Ala Ala Asp Ser Ser Leu Phe Cys Asp Leu Ser Thr
      20             25             30

Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu
      35             40             45

Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
      50             55             60

Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
      65             70             75             80

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Cys	His	Thr	Arg	Ala	Leu	Pro	Gly	Ala	Trp	Val	Lys	Gly	Gln	Ser	Ala	
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Ser Arg Leu His Ala Ala Asp Trp Ala Gly Arg Ala Arg Ala Leu Val
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Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His
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Tyr Gln Ala Val Gly Leu His Leu Trp Lys Val Glu Lys Arg Arg Val
420 425 430

Asn Leu Pro Arg Val Leu Ser Met Pro Pro Val Ala Gly Thr Ala Cys
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His Ala Tyr Asp Arg Glu Val His Leu Arg Cys Glu Leu Ser Pro Gly
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Tyr Tyr Leu Ala Val Pro Ser Thr Phe Leu Lys Asp Ala Pro Gly Glu
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Phe Leu Leu Arg Val Phe Ser Thr Gly Arg Val Ser Leu Arg Ser Gln
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<211> 2204
<212> DNA
<213> Human

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<210> 10
 <211> 444
 <212> PRT
 <213> Human

<400> 10

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Ala Ala Phe Pro Ala Ala Asp Ser Ser Leu Phe Cys Asp Leu Ser Thr
          20             25             30

Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu
          35             40             45

Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
          50             55             60

Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
          65             70             75             80

Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
          85             90             95

Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
          100            105            110

Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu
          115            120            125

Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp
          130            135            140

Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
          145            150            155            160

Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
          165            170            175

Leu Thr Gly Gly Leu Ala Glu Arg Trp Asn Leu Lys Gly Val Ala Gly
          180            185            190

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Ser Gly Gly Gln Gln Asp Arg Pro Gly Arg Trp Glu His Arg Thr Cys
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 Arg Gln Leu Leu His Leu Lys Asp Gln Cys Leu Ile Ser Cys Cys Val
 210 215 220
 Leu Ser Pro Arg Ala Gly Ala Arg Glu Leu Gly Glu Phe His Ala Phe
 225 230 235 240
 Ile Val Ser Asp Leu Arg Glu Leu Gln Gly Gln Ala Gly Gln Cys Ile
 245 250 255
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 260 265 270
 Leu Trp Arg Glu Gly Gly Glu Gly Trp Ser Gln Val Asp Ala Ala Val
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 Cys His Thr Arg Ala Leu Pro Gly Ala Trp Val Lys Gly Gln Ser Ala
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 Gly Gly Cys Arg Asn Asn Ser Gly Phe Pro Ser Asn Pro Lys Phe Trp
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 370 375 380
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 385 390 395 400
 Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His
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 Tyr Gln Ala Val Gly Leu His Leu Trp Lys Gly Val Thr Leu Gly Thr
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 <211> 2516
 <212> DNA
 <213> Human

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 <212> PRT
 <213> Human

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 Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln

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Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly		
	85	90 95
Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg		
	100	105 110
Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu		
	115	120 125
Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp		
	130	135 140
Val Phe Trp Leu Pro Leu Leu Glu Lys Gly Pro Trp Val Leu Arg Ala		
	145	150 155 160
Pro Val Gly Arg Ala Gly Gly Gly Cys Pro Gly Gly Pro Asp Arg Arg		
	165	170 175
Pro Gly Arg Lys Met Glu Pro Glu Gly Arg Ser Arg Lys Arg Arg Pro		
	180	185 190
Ala Gly Gln Ala Arg Pro Leu Gly Ala Gln Asp Leu Ser Ala Ala Ala		
	195	200 205
Pro Pro Glu Gly Pro Val Ser Asp Gln Leu Leu Arg Ala Gln Pro Gln		
	210	215 220
Ser Arg Cys Pro Gly Ala Gly Gly Val Pro Cys Leu His Cys Leu Gly		
	225	230 235 240
Pro Ala Gly Ala Pro Gly Ser Gly Gly Pro Val His Pro Ala Ala Ala		
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Asp Pro Glu Pro Leu Gly Pro Ala Val Leu Ala Gly Ala Leu Glu Arg		
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Gly Gly

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 <211> 2455
 <212> DNA
 <213> Human

<400> 13
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Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
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Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
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Ile Cys Ala Thr Pro Gln Leu Phe Pro Asp Asn Pro Trp Glu Gly Gln

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Thr	Leu	Leu	His	Arg	Val	Val	Pro	His	Gly	Gln	Ser	Phe	Gln	Asn	Gly
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Lys	Ala	Tyr	Ala	Lys	Val	Asn	Gly	Ser	Tyr	Glu	Ala	Leu	Ser	Gly	Gly
		195					200					205			
Ser	Thr	Ser	Glu	Gly	Phe	Glu	Asp	Phe	Thr	Gly	Gly	Val	Thr	Glu	Trp
210						215					220				
Tyr	Glu	Leu	Arg	Lys	Ala	Pro	Ser	Asp	Leu	Tyr	Gln	Ile	Ile	Leu	Lys
225					230					235					240
Ala	Leu	Glu	Arg	Gly	Ser	Leu	Leu	Gly	Cys	Ser	Ile	Asp	Ile	Ser	Ser
				245					250					255	
Val	Leu	Asp	Met	Glu	Ala	Ile	Thr	Phe	Lys	Lys	Leu	Val	Lys	Gly	His
			260					265					270		
Ala	Tyr	Ser	Val	Thr	Gly	Ala	Lys	Gln	Val	Asn	Tyr	Arg	Gly	Gln	Val
		275					280					285			
Val	Ser	Leu	Ile	Arg	Met	Arg	Asn	Pro	Trp	Gly	Glu	Val	Glu	Trp	Thr
	290					295					300				
Gly	Ala	Trp	Ser	Asp	Ser	Ser	Ser	Glu	Trp	Asn	Asn	Val	Asp	Pro	Tyr
305					310					315					320
Glu	Arg	Asp	Gln	Leu	Arg	Val	Lys	Met	Glu	Asp	Gly	Glu	Phe	Trp	Met
				325					330					335	
Ser	Phe	Arg	Asp	Phe	Met	Arg	Glu	Phe	Thr	Arg	Leu	Glu	Ile	Cys	Asn

	645		650		655										
Glu	Leu	Ile	Ile	Thr	Arg	Tyr	Ser	Glu	Pro	Asp	Leu	Ala	Val	Asp	Phe
		660						665					670		
Asp	Asn	Phe	Val	Cys	Cys	Leu	Val	Arg	Leu	Glu	Thr	Met	Phe	Arg	Phe
		675						680				685			
Phe	Lys	Thr	Leu	Asp	Thr	Asp	Leu	Asp	Gly	Val	Val	Thr	Phe	Asp	Leu
		690				695					700				
Phe	Lys	Trp	Leu	Gln	Leu	Thr	Met	Phe	Ala						
705						710									

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 <212> PRT
 <213> Human

<400> 23
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Gly Leu Gly Ser His Glu Arg Ala Ile Lys Tyr Leu Asn Gln Asp Tyr
20 25 30
Glu Ala Leu Arg Asn Glu Cys Leu Glu Ala Gly Thr Leu Phe Gln Asp
35 40 45
Pro Ser Phe Pro Ala Ile Pro Ser Ala Leu Gly Phe Lys Glu Leu Gly
50 55 60
Pro Tyr Ser Ser Lys Thr Arg Gly Met Arg Trp Lys Arg Pro Thr Glu
65 70 75 80
Ile Cys Ala Asp Pro Gln Phe Ile Ile Gly Gly Ala Thr Arg Thr Asp
85 90 95
Ile Cys Gln Gly Ala Leu Gly Asp Cys Trp Leu Leu Ala Ala Ile Ala
100 105 110
Ser Leu Thr Leu Asn Glu Glu Ile Leu Ala Arg Val Val Pro Leu Asn
115 120 125
Gln Ser Phe Gln Glu Asn Tyr Ala Gly Ile Phe His Phe Gln Phe Trp
130 135 140
Gln Tyr Gly Glu Trp Val Glu Val Val Val Asp Asp Arg Leu Pro Thr
145 150 155 160
Lys Asp Gly Glu Leu Leu Phe Val His Ser Ala Glu Gly Ser Glu Phe
165 170 175
Trp Ser Ala Leu Leu Glu Lys Ala Tyr Ala Lys Ile Asn Gly Cys Tyr
180 185 190

Glu	Ala	Leu	Ser	Gly	Gly	Ala	Thr	Thr	Glu	Gly	Phe	Glu	Asp	Phe	Thr	195	200	205
Gly	Gly	Ile	Ala	Glu	Trp	Tyr	Glu	Leu	Lys	Lys	Pro	Pro	Pro	Asn	Leu	210	215	220
Phe	Lys	Ile	Ile	Gln	Lys	Ala	Leu	Gln	Lys	Gly	Ser	Leu	Leu	Gly	Cys	225	230	235
Ser	Ile	Asp	Ile	Thr	Ser	Ala	Ala	Asp	Ser	Glu	Ala	Ile	Thr	Phe	Gln	245	250	255
Lys	Leu	Val	Lys	Gly	His	Ala	Tyr	Ser	Val	Thr	Gly	Ala	Glu	Glu	Val	260	265	270
Glu	Ser	Asn	Gly	Ser	Leu	Gln	Lys	Leu	Ile	Arg	Ile	Arg	Asn	Pro	Trp	275	280	285
Gly	Glu	Val	Glu	Trp	Thr	Gly	Arg	Trp	Asn	Asp	Asn	Cys	Pro	Ser	Trp	290	295	300
Asn	Thr	Ile	Asp	Pro	Glu	Glu	Arg	Glu	Arg	Leu	Thr	Arg	Arg	His	Glu	305	310	315
Asp	Gly	Glu	Phe	Trp	Met	Ser	Phe	Ser	Asp	Phe	Leu	Arg	His	Tyr	Ser	325	330	335
Arg	Leu	Glu	Ile	Cys	Asn	Leu	Thr	Pro	Asp	Thr	Leu	Thr	Ser	Asp	Thr	340	345	350
Tyr	Lys	Lys	Trp	Lys	Leu	Thr	Lys	Met	Asp	Gly	Asn	Trp	Arg	Arg	Gly	355	360	365
Ser	Thr	Ala	Gly	Gly	Cys	Arg	Asn	Tyr	Pro	Asn	Thr	Phe	Trp	Met	Asn	370	375	380
Pro	Gln	Tyr	Leu	Ile	Lys	Leu	Glu	Glu	Glu	Asp	Glu	Asp	Glu	Glu	Asp	385	390	395
Gly	Glu	Ser	Gly	Cys	Thr	Phe	Leu	Val	Gly	Leu	Ile	Gln	Lys	His	Arg	405	410	415
Arg	Arg	Gln	Arg	Lys	Met	Gly	Glu	Asp	Met	His	Thr	Ile	Gly	Phe	Gly	420	425	430
Ile	Tyr	Glu	Val	Pro	Glu	Glu	Leu	Ser	Gly	Gln	Thr	Asn	Ile	His	Leu	435	440	445
Ser	Lys	Asn	Phe	Phe	Leu	Thr	Asn	Arg	Ala	Arg	Glu	Arg	Ser	Asp	Thr	450	455	460
Phe	Ile	Asn	Leu	Arg	Glu	Val	Leu	Asn	Arg	Phe	Lys	Leu	Pro	Pro	Gly	465	470	475
Glu	Tyr	Ile	Leu	Val	Pro	Ser	Thr	Phe	Glu	Pro	Asn	Lys	Asp	Gly	Asp	485	490	495

Phe Cys Ile Arg Val Phe Ser Glu Lys Lys Ala Asp Tyr Gln Ala Val
 500 505 510
 Asp Asp Glu Ile Glu Ala Asn Leu Glu Glu Phe Asp Ile Ser Glu Asp
 515 520 525
 Asp Ile Asp Asp Gly Val Arg Arg Leu Phe Ala Gln Leu Ala Gly Glu
 530 535 540
 Asp Ala Glu Ile Ser Ala Phe Glu Leu Gln Thr Ile Leu Arg Arg Val
 545 550 555 560
 Leu Ala Lys Arg Gln Asp Ile Lys Ser Asp Gly Phe Ser Ile Glu Thr
 565 570 575
 Cys Lys Ile Met Val Asp Met Leu Asp Ser Asp Gly Ser Gly Lys Leu
 580 585 590
 Gly Leu Lys Glu Phe Tyr Ile Leu Trp Thr Lys Ile Gln Lys Tyr Gln
 595 600 605
 Lys Ile Tyr Arg Glu Ile Asp Val Asp Arg Ser Gly Thr Met Asn Ser
 610 615 620
 Tyr Glu Met Arg Lys Ala Leu Glu Glu Ala Gly Phe Lys Met Pro Cys
 625 630 635 640
 Gln Leu His Gln Val Ile Val Ala Arg Phe Ala Asp Asp Gln Leu Ile
 645 650 655
 Ile Asp Phe Asp Asn Phe Val Arg Cys Leu Val Arg Leu Glu Thr Leu
 660 665 670
 Phe Lys Ile Phe Lys Gln Leu Asp Pro Glu Asn Thr Gly Thr Ile Glu
 675 680 685
 Leu Asp Leu Ile Ser Trp Leu Cys Phe Ser Val Leu
 690 695 700

<210> 24
 <211> 821
 <212> PRT
 <213> Human

<400> 24

Met Pro Thr Val Ile Ser Ala Ser Val Ala Pro Arg Thr Ala Ala Glu
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 Pro Arg Ser Pro Gly Pro Val Pro His Pro Ala Gln Ser Lys Ala Thr
 20 25 30
 Glu Ala Gly Gly Gly Asn Pro Ser Gly Ile Tyr Ser Ala Ile Ile Ser
 35 40 45
 Arg Asn Phe Pro Ile Ile Gly Val Lys Glu Lys Thr Phe Glu Gln Leu
 50 55 60

His	Lys	Lys	Cys	Leu	Glu	Lys	Lys	Val	Leu	Tyr	Val	Asp	Pro	Glu	Phe	65	70	75	80
Pro	Pro	Asp	Glu	Thr	Ser	Leu	Phe	Tyr	Ser	Gln	Lys	Phe	Pro	Ile	Gln	85	90	95	
Phe	Val	Trp	Lys	Arg	Pro	Pro	Glu	Ile	Cys	Glu	Asn	Pro	Arg	Phe	Ile	100	105	110	
Ile	Asp	Gly	Ala	Asn	Arg	Thr	Asp	Ile	Cys	Gln	Gly	Glu	Leu	Gly	Asp	115	120	125	
Cys	Trp	Phe	Leu	Ala	Ala	Ile	Ala	Cys	Leu	Thr	Leu	Asn	Gln	His	Leu	130	135	140	
Leu	Phe	Arg	Val	Ile	Pro	His	Asp	Gln	Ser	Phe	Ile	Glu	Asn	Tyr	Ala	145	150	155	160
Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	Arg	Tyr	Gly	Glu	Trp	Val	Asp	Val	165	170	175	
Val	Ile	Asp	Asp	Cys	Leu	Pro	Thr	Tyr	Asn	Asn	Gln	Leu	Val	Phe	Thr	180	185	190	
Lys	Ser	Asn	His	Arg	Asn	Glu	Phe	Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	195	200	205	
Tyr	Ala	Lys	Leu	His	Gly	Ser	Tyr	Glu	Ala	Leu	Lys	Gly	Gly	Asn	Thr	210	215	220	
Thr	Glu	Ala	Met	Glu	Asp	Phe	Thr	Gly	Gly	Val	Ala	Glu	Phe	Phe	Glu	225	230	235	240
Ile	Arg	Asp	Ala	Pro	Ser	Asp	Met	Tyr	Lys	Ile	Met	Lys	Lys	Ala	Ile	245	250	255	
Glu	Arg	Gly	Ser	Leu	Met	Gly	Cys	Ser	Ile	Asp	Asp	Gly	Thr	Asn	Met	260	265	270	
Thr	Tyr	Gly	Thr	Ser	Pro	Ser	Gly	Leu	Asn	Met	Gly	Glu	Leu	Ile	Ala	275	280	285	
Arg	Met	Val	Arg	Asn	Met	Asp	Asn	Ser	Leu	Leu	Gln	Asp	Ser	Asp	Leu	290	295	300	
Asp	Pro	Arg	Gly	Ser	Asp	Glu	Arg	Pro	Thr	Arg	Thr	Ile	Ile	Pro	Val	305	310	315	320
Gln	Tyr	Glu	Thr	Arg	Met	Ala	Cys	Gly	Leu	Val	Arg	Gly	His	Ala	Tyr	325	330	335	
Ser	Val	Thr	Gly	Leu	Asp	Glu	Val	Pro	Phe	Lys	Gly	Glu	Lys	Val	Lys	340	345	350	
Leu	Val	Arg	Leu	Arg	Asn	Pro	Trp	Gly	Gln	Val	Glu	Trp	Asn	Gly	Ser	355	360	365	

Trp	Ser	Asp	Arg	Trp	Lys	Asp	Trp	Ser	Phe	Val	Asp	Lys	Asp	Glu	Lys	
370						375					380					
Ala	Arg	Leu	Gln	His	Gln	Val	Thr	Glu	Asp	Gly	Glu	Phe	Trp	Met	Ser	
385					390					395					400	
Tyr	Glu	Asp	Phe	Ile	Tyr	His	Phe	Thr	Lys	Leu	Glu	Ile	Cys	Asn	Leu	
				405					410					415		
Thr	Ala	Asp	Ala	Leu	Gln	Ser	Asp	Lys	Leu	Gln	Thr	Trp	Thr	Val	Ser	
			420					425						430		
Val	Asn	Glu	Gly	Arg	Trp	Val	Arg	Gly	Cys	Ser	Ala	Gly	Gly	Cys	Arg	
		435					440					445				
Asn	Phe	Pro	Asp	Thr	Phe	Trp	Thr	Asn	Pro	Gln	Tyr	Arg	Leu	Lys	Leu	
	450					455					460					
Leu	Glu	Glu	Asp	Asp	Asp	Pro	Asp	Asp	Ser	Glu	Val	Ile	Cys	Ser	Phe	
465					470					475					480	
Leu	Val	Ala	Leu	Met	Gln	Lys	Asn	Arg	Arg	Lys	Asp	Arg	Lys	Leu	Gly	
				485					490					495		
Ala	Ser	Leu	Phe	Thr	Ile	Gly	Phe	Ala	Ile	Tyr	Glu	Val	Pro	Lys	Glu	
			500					505						510		
Met	His	Gly	Asn	Lys	Gln	His	Leu	Gln	Lys	Asp	Phe	Phe	Leu	Tyr	Asn	
		515					520					525				
Ala	Ser	Lys	Ala	Arg	Ser	Lys	Thr	Tyr	Ile	Asn	Met	Arg	Glu	Val	Ser	
		530				535					540					
Gln	Arg	Phe	Arg	Leu	Pro	Pro	Ser	Glu	Tyr	Val	Ile	Val	Pro	Ser	Thr	
545					550					555					560	
Tyr	Glu	Pro	His	Gln	Glu	Gly	Glu	Phe	Ile	Leu	Arg	Val	Phe	Ser	Glu	
				565					570					575		
Lys	Arg	Asn	Leu	Ser	Glu	Glu	Val	Glu	Asn	Thr	Ile	Ser	Val	Asp	Arg	
			580					585					590			
Pro	Val	Lys	Lys	Lys	Lys	Thr	Lys	Pro	Ile	Ile	Phe	Val	Ser	Asp	Arg	
		595					600					605				
Ala	Asn	Ser	Asn	Lys	Glu	Leu	Gly	Val	Asp	Gln	Glu	Ser	Glu	Glu	Gly	
	610					615					620					
Lys	Gly	Lys	Thr	Ser	Pro	Asp	Lys	Gln	Lys	Gln	Ser	Pro	Gln	Pro	Gln	
625					630					635					640	
Pro	Gly	Ser	Ser	Asp	Gln	Glu	Ser	Glu	Glu	Gln	Gln	Gln	Phe	Arg	Asn	
				645					650					655		
Ile	Phe	Lys	Gln	Ile	Ala	Gly	Asp	Asp	Met	Glu	Ile	Cys	Ala	Asp	Glu	
			660					665						670		

Leu Lys Lys Val Leu Asn Thr Val Val Asn Lys His Lys Asp Leu Lys
 675 680 685
 Thr His Gly Phe Thr Leu Glu Ser Cys Arg Ser Met Ile Ala Leu Met
 690 695 700
 Asp Thr Asp Gly Ser Gly Lys Leu Asn Leu Gln Glu Phe His His Leu
 705 710 715 720
 Trp Asn Lys Ile Lys Ala Trp Gln Lys Ile Phe Lys His Tyr Asp Thr
 725 730 735
 Asp Gln Ser Gly Thr Ile Asn Ser Tyr Glu Met Arg Asn Ala Val Asn
 740 745 750
 Asp Ala Gly Phe His Leu Asn Asn Gln Leu Tyr Asp Ile Ile Thr Met
 755 760 765
 Arg Tyr Ala Asp Lys His Met Asn Ile Asp Phe Asp Ser Phe Ile Cys
 770 775 780
 Cys Phe Val Arg Leu Glu Gly Met Phe Arg Ala Phe His Ala Phe Asp
 785 790 795 800
 Lys Asp Gly Asp Gly Ile Ile Lys Leu Asn Val Leu Glu Trp Leu Gln
 805 810 815
 Leu Thr Met Tyr Ala
 820
 <210> 25
 <211> 639
 <212> PRT
 <213> Human
 <400> 25
 Met Phe Ser Cys Val Lys Pro Tyr Glu Asp Gln Asn Tyr Ser Ala Leu
 1 5 10 15
 Arg Arg Asp Cys Arg Arg Arg Lys Val Leu Phe Glu Asp Pro Leu Phe
 20 25 30
 Pro Ala Thr Asp Asp Ser Leu Tyr Tyr Lys Gly Thr Pro Gly Pro Ala
 35 40 45
 Val Arg Arg Lys Arg Pro Lys Gly Ile Cys Glu Asp Pro Arg Leu Phe
 50 55 60
 Val Asp Gly Ile Ser Ser His Asp Leu His Gln Gly Gln Val Gly Asn
 65 70 75 80
 Cys Trp Phe Val Ala Ala Cys Ser Ser Leu Ala Ser Arg Glu Ser Leu
 85 90 95
 Trp Gln Lys Val Ile Pro Asp Trp Lys Glu Gln Glu Trp Asp Pro Glu

100					105					110					
Lys	Pro	Asn	Ala	Tyr	Ala	Gly	Ile	Phe	His	Phe	His	Phe	Trp	Arg	Phe
		115					120					125			
Gly	Trp	Val	Asp	Val	Val	Ile	Asp	Asp	Arg	Leu	Pro	Thr	Val	Asn	Asn
	130					135					140				
Gln	Leu	Ile	Tyr	Cys	His	Ser	Asn	Ser	Arg	Asn	Glu	Phe	Trp	Cys	Ala
145					150					155					160
Leu	Val	Glu	Lys	Ala	Tyr	Ala	Lys	Leu	Ala	Gly	Cys	Tyr	Gln	Ala	Leu
				165					170					175	
Asp	Gly	Gly	Asn	Thr	Ala	Asp	Ala	Leu	Val	Asp	Phe	Thr	Gly	Gly	Val
			180					185					190		
Ser	Glu	Pro	Ile	Asp	Leu	Thr	Glu	Gly	Asp	Phe	Ala	Asn	Asp	Glu	Thr
		195					200					205			
Lys	Arg	Asn	Gln	Leu	Phe	Glu	Arg	Met	Leu	Lys	Val	His	Ser	Arg	Gly
	210					215					220				
Gly	Leu	Ile	Ser	Ala	Ser	Ile	Lys	Ala	Val	Thr	Ala	Ala	Asp	Met	Glu
225					230					235					240
Ala	Arg	Leu	Ala	Cys	Gly	Leu	Val	Lys	Gly	His	Ala	Tyr	Ala	Val	Thr
				245					250					255	
Asp	Val	Arg	Lys	Val	Arg	Leu	Gly	His	Gly	Leu	Leu	Ala	Phe	Phe	Lys
			260					265					270		
Ser	Glu	Lys	Leu	Asp	Met	Ile	Arg	Leu	Arg	Asn	Pro	Trp	Gly	Glu	Arg
		275					280					285			
Glu	Trp	Asn	Gly	Pro	Trp	Ser	Asp	Thr	Ser	Glu	Glu	Trp	Gln	Lys	Val
	290					295					300				
Ser	Lys	Ser	Glu	Arg	Glu	Lys	Met	Gly	Val	Thr	Val	Gln	Asp	Asp	Gly
305					310					315					320
Glu	Phe	Trp	Met	Thr	Phe	Glu	Asp	Val	Cys	Arg	Tyr	Phe	Thr	Asp	Ile
				325					330					335	
Ile	Lys	Cys	Arg	Val	Ile	Asn	Thr	Ser	His	Leu	Ser	Ile	His	Lys	Thr
			340					345					350		
Trp	Glu	Glu	Ala	Arg	Leu	His	Gly	Ala	Trp	Thr	Leu	His	Glu	Asp	Pro
		355					360					365			
Arg	Gln	Asn	Arg	Gly	Gly	Gly	Cys	Ile	Asn	His	Lys	Asp	Thr	Phe	Phe
	370					375					380				
Gln	Asn	Pro	Gln	Tyr	Ile	Phe	Glu	Val	Lys	Lys	Pro	Glu	Asp	Glu	Val
385					390					395					400
Leu	Ile	Cys	Ile	Gln	Gln	Arg	Pro	Lys	Arg	Ser	Thr	Arg	Arg	Glu	Gly

				405						410					415			
Lys	Gly	Glu	Asn	Leu	Ala	Ile	Gly	Phe	Asp	Ile	Tyr	Lys	Val	Glu	Glu			
			420					425					430					
Asn	Arg	Gln	Tyr	Arg	Met	His	Ser	Leu	Gln	His	Lys	Ala	Ala	Ser	Ser			
		435					440					445						
Ile	Tyr	Ile	Asn	Ser	Arg	Ser	Val	Phe	Leu	Arg	Thr	Asp	Gln	Pro	Glu			
	450					455					460							
Gly	Arg	Tyr	Val	Ile	Ile	Pro	Thr	Thr	Phe	Glu	Pro	Gly	His	Thr	Gly			
465					470					475					480			
Glu	Phe	Leu	Leu	Arg	Val	Phe	Thr	Asp	Val	Pro	Ser	Asn	Cys	Arg	Glu			
				485					490					495				
Leu	Arg	Leu	Asp	Glu	Pro	Pro	His	Thr	Cys	Trp	Ser	Ser	Leu	Cys	Gly			
			500					505					510					
Tyr	Pro	Gln	Leu	Val	Thr	Gln	Val	His	Val	Leu	Gly	Ala	Ala	Gly	Leu			
		515					520					525						
Lys	Asp	Ser	Pro	Thr	Gly	Ala	Asn	Ser	Tyr	Val	Ile	Ile	Lys	Cys	Glu			
	530					535					540							
Gly	Asp	Lys	Val	Arg	Ser	Ala	Val	Gln	Lys	Gly	Thr	Ser	Thr	Pro	Glu			
545					550					555					560			
Tyr	Asn	Val	Lys	Gly	Ile	Phe	Tyr	Arg	Lys	Lys	Leu	Ser	Gln	Pro	Ile			
				565					570					575				
Thr	Val	Gln	Val	Trp	Asn	His	Arg	Val	Leu	Lys	Asp	Glu	Phe	Leu	Gly			
			580					585					590					
Gln	Val	His	Leu	Lys	Ala	Asp	Pro	Asp	Asn	Leu	Gln	Ala	Leu	His	Thr			
		595					600					605						
Leu	His	Leu	Arg	Asp	Arg	Asn	Ser	Arg	Gln	Pro	Ser	Asn	Leu	Pro	Gly			
	610					615					620							
Thr	Val	Ala	Val	His	Ile	Leu	Ser	Ser	Thr	Ser	Leu	Met	Ala	Val				
625					630					635								

<210> 26
 <211> 641
 <212> PRT
 <213> Mus musculus

<400> 26
 Met Gly Pro Pro Leu Lys Leu Phe Lys Asn Gln Lys Tyr Gln Glu Leu
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 Lys Gln Glu Cys Met Lys Asp Gly Arg Leu Phe Cys Asp Pro Thr Phe
 20 25 30

Leu Asn Val Cys Arg Asn Val Asn Asn Pro Val Phe Gly Arg Lys Glu
 340 345 350
 Leu Glu Ser Val Val Gly Cys Trp Thr Val Asp Asp Asp Pro Leu Met
 355 360 365
 Asn Arg Ser Gly Gly Cys Tyr Asn Asn Arg Asp Thr Phe Leu Gln Asn
 370 375 380
 Pro Gln Tyr Ile Phe Thr Val Pro Glu Asp Gly His Lys Val Ile Met
 385 390 395 400
 Ser Leu Gln Gln Lys Asp Leu Arg Thr Tyr Arg Arg Met Gly Arg Pro
 405 410 415
 Asp Asn Tyr Ile Ile Gly Phe Glu Leu Phe Lys Val Glu Met Asn Arg
 420 425 430
 Arg Phe Arg Leu His His Leu Tyr Ile Gln Glu Arg Ala Gly Thr Ser
 435 440 445
 Thr Tyr Ile Asp Thr Arg Thr Val Phe Leu Ser Lys Tyr Leu Lys Lys
 450 455 460
 Gly Ser Tyr Val Leu Val Pro Thr Met Phe Gln His Gly Arg Thr Ser
 465 470 475 480
 Glu Phe Leu Leu Arg Ile Phe Ser Glu Val Pro Val Gln Leu Arg Glu
 485 490 495
 Leu Thr Leu Asp Met Pro Lys Met Ser Cys Trp Asn Leu Ala Arg Gly
 500 505 510
 Tyr Pro Lys Val Val Thr Gln Ile Thr Val His Ser Ala Glu Gly Leu
 515 520 525
 Glu Lys Lys Tyr Ala Asn Glu Thr Val Asn Pro Tyr Leu Ile Ile Lys
 530 535 540
 Cys Gly Lys Glu Glu Val Arg Ser Pro Val Gln Lys Asn Thr Val His
 545 550 555 560
 Ala Ile Phe Asp Thr Gln Ala Val Phe Tyr Arg Arg Thr Thr Asp Ile
 565 570 575
 Pro Ile Ile Ile Gln Val Trp Asn Ser Arg Lys Phe Cys Asp Gln Phe
 580 585 590
 Leu Gly Gln Val Thr Leu Asp Ala Asp Pro Ser Asp Cys Arg Asp Leu
 595 600 605
 Lys Ser Leu Tyr Leu Arg Lys Lys Gly Gly Pro Thr Ala Lys Val Lys
 610 615 620
 Gln Gly His Ile Ser Phe Lys Val Ile Ser Ser Asp Asp Leu Thr Glu
 625 630 635 640

Leu

<210> 27
<211> 703
<212> PRT
<213> RAT

<400> 27

Met	Ala	Ala	Leu	Ala	Ala	Gly	Val	Ser	Lys	Gln	Arg	Ala	Val	Ala	Glu	
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Gly	Leu	Gly	Ser	Asn	Gln	Asn	Ala	Val	Lys	Tyr	Leu	Gly	Gln	Asp	Phe	
			20					25					30			
Glu	Thr	Leu	Arg	Lys	Gln	Cys	Leu	Asn	Ser	Gly	Val	Leu	Phe	Lys	Asp	
		35					40					45				
Pro	Glu	Phe	Pro	Ala	Cys	Pro	Ser	Ala	Leu	Gly	Tyr	Lys	Asp	Leu	Gly	
	50					55					60					
Pro	Gly	Ser	Pro	Asp	Thr	Gln	Gly	Ile	Val	Trp	Lys	Arg	Pro	Thr	Glu	
	65				70					75					80	
Leu	Cys	Pro	Asn	Pro	Gln	Phe	Ile	Val	Gly	Gly	Ala	Thr	Arg	Thr	Asp	
				85					90					95		
Ile	Arg	Gln	Gly	Gly	Leu	Gly	Asp	Cys	Trp	Leu	Leu	Ala	Ala	Ile	Ala	
		100						105					110			
Ser	Leu	Thr	Leu	Asn	Glu	Lys	Leu	Leu	Tyr	Arg	Val	Leu	Pro	Arg	Asp	
		115					120					125				
Gln	Ser	Phe	Gln	Lys	Asp	Tyr	Ala	Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	
	130					135					140					
Gln	Tyr	Gly	Glu	Trp	Val	Glu	Val	Val	Ile	Asp	Asp	Arg	Leu	Pro	Thr	
	145				150					155					160	
Lys	Asn	Gly	Gln	Leu	Leu	Phe	Leu	His	Ser	Glu	Glu	Gly	Asn	Glu	Phe	
			165					170						175		
Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	Tyr	Ala	Lys	Leu	Asn	Gly	Ser	Tyr	
		180						185					190			
Glu	Ala	Leu	Val	Gly	Gly	Ser	Thr	Ile	Glu	Gly	Phe	Glu	Asp	Phe	Thr	
		195					200					205				
Gly	Gly	Ile	Ser	Glu	Phe	Tyr	Asp	Leu	Lys	Lys	Pro	Pro	Glu	Asn	Leu	
	210					215					220					
Tyr	Tyr	Ile	Ile	Gln	Lys	Ala	Leu	Arg	Lys	Gly	Ser	Leu	Leu	Gly	Cys	
	225				230					235					240	
Ser	Ile	Asp	Val	Ser	Thr	Ala	Ala	Glu	Ala	Glu	Ala	Thr	Thr	Arg	Gln	
			245					250						255		

Lys	Leu	Val	Lys	Gly	His	Ala	Tyr	Ser	Val	Thr	Gly	Val	Glu	Glu	Val			
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Asn	Phe	His	Gly	Arg	Pro	Glu	Lys	Leu	Ile	Arg	Leu	Arg	Asn	Pro	Trp			
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Gly	Glu	Val	Glu	Trp	Ser	Gly	Ala	Trp	Ser	Asp	Asn	Ala	Pro	Glu	Trp			
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Ile	His	Lys	Trp	Asn	Leu	Val	Leu	Phe	Asn	Gly	Arg	Trp	Thr	Arg	Gly			
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	370					375					380							
Pro	Gln	Phe	Lys	Ile	His	Leu	Asp	Glu	Val	Asp	Glu	Asp	Gln	Glu	Glu			
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Gly	Thr	Ser	Glu	Pro	Cys	Cys	Thr	Val	Leu	Leu	Gly	Leu	Met	Gln	Lys			
				405					410					415				
Asn	Arg	Arg	Arg	Gln	Lys	Arg	Ile	Gly	Gln	Gly	Met	Leu	Ser	Ile	Gly			
			420					425					430					
Tyr	Ala	Val	Tyr	Gln	Ile	Pro	Lys	Glu	Leu	Glu	Ser	His	Thr	Asp	Ala			
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Ser	Thr	Tyr	Met	Asn	Leu	Arg	Glu	Val	Ser	Ser	Arg	Val	Arg	Leu	Pro			
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Pro	Gly	Gln	Tyr	Leu	Val	Val	Pro	Ser	Thr	Phe	Glu	Pro	Phe	Lys	Asp			
				485					490					495				
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Asn Glu Val Leu Ser Lys Arg Thr Asp Met Lys Phe Asp Gly Phe Asn
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Ile Asn Thr Cys Arg Glu Met Ile Ser Leu Leu Asp Ser Asp Gly Thr
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Gly Ser Leu Gly Pro Met Glu Phe Lys Thr Leu Trp Leu Lys Ile Arg
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Thr Tyr Leu Glu Ile Phe Gln Glu Met Asp His Asn His Val Gly Thr
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Ile Glu Ala His Glu Met Arg Thr Ala Leu Lys Lys Ala Gly Phe Thr
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Leu Asn Asn Gln Val Gln Gln Thr Ile Ala Met Arg Tyr Ala Cys Ser
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Lys Leu Gly Val Asp Phe Asn Gly Phe Val Ala Cys Met Ile Arg Leu
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Pro Ala Ser Asn Ser Ser Leu Phe Tyr Ser Glu Arg Pro Gln Ile Pro
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Phe Val Trp Lys Arg Pro Gly Glu Ile Val Lys Asn Pro Glu Phe Ile
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Leu Gly Gly Ala Thr Arg Thr Asp Ile Cys Gln Gly Glu Leu Gly Asp
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Cys Trp Leu Leu Ala Ala Ile Ala Ser Leu Thr Leu Asn Gln Lys Ala
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Leu Ala Arg Val Ile Pro Gln Asp Gln Ser Phe Gly Pro Gly Tyr Ala

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His	Ser	Ala	Asp	His	Asn	Glu	Phe	Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala
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Tyr	Ala	Lys	Leu	Asn	Gly	Ser	Tyr	Glu	Ala	Leu	Lys	Gly	Gly	Ser	Ala
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Ser	Val	Thr	Gly	Ile	Asp	Gln	Val	Ser	Phe	Arg	Gly	Gln	Arg	Ile	Glu
			260					265					270		
Leu	Ile	Arg	Ile	Arg	Asn	Pro	Trp	Gly	Gln	Val	Glu	Trp	Asn	Gly	Ser
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Trp	Ser	Asp	Ser	Ser	Pro	Glu	Trp	Arg	Ser	Val	Gly	Pro	Ala	Glu	Gln
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Lys	Arg	Leu	Cys	His	Thr	Ala	Leu	Asp	Asp	Gly	Glu	Phe	Trp	Met	Ala
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Phe	Lys	Asp	Phe	Lys	Ala	His	Phe	Asp	Lys	Val	Glu	Ile	Cys	Asn	Leu
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Val	His	Gln	Gly	Ser	Trp	Val	Arg	Gly	Ser	Thr	Ala	Gly	Gly	Cys	Arg
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Asn	Phe	Leu	Asp	Thr	Phe	Trp	Thr	Asn	Pro	Gln	Ile	Lys	Leu	Ser	Leu
	370					375					380				
Thr	Glu	Lys	Asp	Glu	Gly	Gln	Glu	Glu	Cys	Ser	Phe	Leu	Val	Ala	Leu
385					390					395					400
Met	Gln	Lys	Asp	Arg	Arg	Lys	Leu	Lys	Arg	Phe	Gly	Ala	Asn	Val	Leu
				405					410					415	
Thr	Ile	Gly	Tyr	Ala	Ile	Tyr	Glu	Cys	Pro	Asp	Lys	Asp	Glu	His	Leu

420					425					430					
Asn	Lys	Asp	Phe	Phe	Arg	Tyr	His	Ala	Ser	Arg	Ala	Arg	Ser	Lys	Thr
		435					440					445			
Phe	Ile	Asn	Leu	Arg	Glu	Val	Ser	Asp	Arg	Phe	Lys	Leu	Pro	Pro	Gly
	450					455					460				
Glu	Tyr	Ile	Leu	Ile	Pro	Ser	Thr	Phe	Glu	Pro	His	Gln	Glu	Ala	Asp
465					470					475					480
Phe	Cys	Leu	Arg	Ile	Phe	Ser	Glu	Lys	Lys	Ala	Ile	Thr	Arg	Asp	Met
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Asp	Gly	Asn	Val	Asp	Ile	Asp	Leu	Pro	Glu	Pro	Pro	Lys	Pro	Thr	Pro
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Pro	Asp	Gln	Glu	Thr	Glu	Glu	Glu	Gln	Arg	Phe	Arg	Ala	Leu	Phe	Glu
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Gln	Val	Ala	Gly	Glu	Asp	Met	Glu	Val	Thr	Ala	Glu	Glu	Leu	Glu	Tyr
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Val	Leu	Asn	Ala	Val	Leu	Gln	Lys	Lys	Lys	Asp	Ile	Lys	Phe	Lys	Lys
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Leu	Ser	Leu	Ile	Ser	Cys	Lys	Asn	Ile	Ile	Ser	Leu	Met	Asp	Thr	Ser
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Gly	Asn	Gly	Lys	Leu	Glu	Phe	Asp	Glu	Phe	Lys	Val	Phe	Trp	Asp	Lys
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Leu	Lys	Gln	Trp	Ile	Asn	Leu	Phe	Leu	Arg	Phe	Asp	Ala	Asp	Lys	Ser
		595					600					605			
Gly	Thr	Met	Ser	Thr	Tyr	Glu	Leu	Arg	Thr	Ala	Leu	Lys	Ala	Ala	Gly
	610					615					620				
Phe	Gln	Leu	Ser	Ser	His	Leu	Leu	Gln	Leu	Ile	Val	Leu	Arg	Tyr	Ala
625					630					635					640
Asp	Glu	Glu	Leu	Gln	Leu	Asp	Phe	Asp	Asp	Phe	Leu	Asn	Cys	Leu	Val
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Arg	Leu	Glu	Asn	Ala	Ser	Arg	Val	Phe	Gln	Ala	Leu	Ser	Thr	Lys	Asn
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Lys	Glu	Phe	Ile	His	Leu	Asn	Ile	Asn	Glu	Phe	Ile	His	Leu	Thr	Met
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Primer

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